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Government of India
Ministry of Health and Family Welfare
National AIDS Control Organisation
Department of AIDS Control

6th & 9th Floor, Chandralok Building
36, Janpath, New Delhi
Dated: 27th, January, 2015

Office Memorandum

Please find enclosed the minutes of Core Group on HIV and Kala azar held on 1st September, 2014 at RMI, Patna.

Yours faithfully,

(Dr. A.S. Rathore)
DDG (CST)
Ph: 23731805

Minutes of the first meeting of working group on HIV and Kala-azar in India

The first meeting of HIV-Kala-azar working group was held at RMRIMS, Patna on 1st of September 2014. The working group has been constituted by NACO along with NVBDCP. The following members were present:

1. Dr. Shyam Sundar, Professor & Head, BHU, Varanasi (Chairperson)
2. Dr. A. C. Dhariwal, Director, NVBDCP (Co- Chairperson)
3. Dr. A. S. Rathore, DDG (CST), NACO (Co- Chairperson)
4. Dr. B. B. Rewari, NPO (ART), WHO India (Member Secretary)
5. Dr. Pradeep Das, Director, RMRIS, Patna
6. Dr. Prabhat Kumar Sinha, Dy. Director, RMRIMS, Patna
7. Dr. Krishna Pandey, Dy. Director, RMRIMS, Patna
8. Dr. R. K. Goswami, STM, Kolkatta
9. Dr. Saurabh Jain, WHO, India
10. Dr. Sakib Burza, MSF
11. Dr. Temmy Sunyoto, MSF
12. Mr. Mithilesh Pandey, AD (ICTC), BSACS

At the outset, the Director of the Institute Dr. Pradeep Das welcomed the participants for this important meeting. The chairperson in his opening remarks congratulated NACO and NVBDCP for taking this initiative, particularly at a time when Government of India is focussing on Kala-azar elimination. The member secretary then gave an overview of the agenda for the day **(Annexure - I)**

Setting the tone of meeting, Dr. Rathore emphasized on the need for HIV detection among patients with Visceral Leishmaniasis (VL) considering that recent studies from Bihar have shown 2 to 5 per cent positivity. Dr. Dhariwal opined that this meeting is coming at very opportune time as the Government is going to announce the launch of Ambisome in the Kala-azar programme tomorrow. It will be quite useful to have inputs from this group discussion to feed into testing and treatment guidelines for HIV-VL co-infected patients.

This was followed by presentation by Dr. Pradeep Das, who gave an overview of current situation of VL in India with particular reference to Bihar. He informed that Kala-azar is endemic in 4 states in India, total 54 districts - 33 districts in Bihar, 11 West Bengal, 4 Jharkhand and 6 in Uttar Pradesh. However, 80% of total cases are in Bihar. The focus is on elimination in 195 blocks where there are more than 1 case per 10,000 population.

Dr. B. B. Rewari gave an overview of the current status of HIV in India and the success achieved in terms of reduction of new infections and deaths due to HIV/AIDS. He also

gave an overview of HIV situation in Bihar. He informed that there are 466 HIV testing sites, 16 ART centres and 9 Care and Support centre in Bihar. The overall prevalence of HIV in Bihar is 0.23 per cent.

Dr. Sakib Burza stated that MSF in collaboration with RMRIMS has been treating VL patients with Ambisome since 2007. Routine testing for HIV in all VL patients showed a positivity of 2.4%. HIV-VL co-infected patients were being treated with a dose of 20-25 mg/kg of Ambisome. The relapse rate was 16 per cent in the first year after treatment. WHO recommendation is for a dose of 40 mg/kg of Ambisome for HIV-VL. With this dose the relapses have been found to be much less. The lost to follow-up cases have to be traced and taken care of. VL should be made as a AIDS defining condition.

Dr. P. K. Sinha focussed on the diagnosis of VL particularly in co-infected patients. RDT (rk-39) particularly in cases of co-infection is positive in about 86 per cent of the cases in the RMRIMS study. In these cases (14%) confirmation can only be done by spleenic/bone marrow aspiration. However spleenic aspiration is ethically and technically difficult in the field condition due to lack of technical expertise and proper laboratory facility. HIV testing is done three rapid tests and CD_4 counts to assess the immunological status of the co-infected patients.

Dr. Krishna Pandey discussed the various drugs used for the treatment of VL. He added that RMRIMS in collaboration with MSF has treated more than 150 patients with Ambisome in the dose of 20mg/kg. The results have been extremely good with a very high initial cure rate and almost negligible side effects. Drug combinations such as Ambisome + Miltefosine, Ambisome + Paramomycin and Miltefosine + Paramomycin though quite effective in VL have not been tried in co-infected patients. Miltefosine was given in 6 patients with good initial cure rate. However, relapses occurred quite frequently.

Dr. Shyam Sundar dealt with the national guidelines on ART treatment. He stated that tenofovir had a nephrotoxicity of about 3 per cent. Zidovudine was not to be given in patients with bone marrow depression and anaemia less than 9gm/dl. He also dealt with the toxic effects of ARV drugs.

Dr. Saurabh Jain talked about some of the studies relating to WHO guidelines on HIV-VL co-infection. Only about 40-50 per cent co-infected patients detect specific antibody for VL. So, two different antigen kits should be used. A total dose of 40mg/kg of Ambisome has been recommended by WHO for treatment of co-infected patients. Where ART was not used early the relapse rate was as high as 60% in 6-9 months and 90 per cent in 12 months. The same ART used for HIV has to be employed for co-infected patients. There is no role of secondary prophylaxis in co-infected patients.

Dr. B. B. Rewari, then outlined the following key questions to be discussed and recommendations be made accordingly. This was followed by discussions on the key questions and sharing of experience from the experts. Considering the vast experience of Dr. P. Das, Director RMRI, it was decided to include him in the HIV-Kala-azar working group. The questions and answers to these as discussed in the meeting and e-exchange following the meeting are as below:

Question 1. Testing for HIV in VL patients?

Answer Considering that 2-5.6% of VL patients may be co-infected with HIV, it was recommended that all patients who **are diagnosed with VL** (rk-39 positive (RDT for VL or otherwise) should be "offered" HIV testing with appropriate linkage to ICTC/F-ICTC where counselling and testing for HIV should be done with informed consent as per national guidelines. These will be done across the country but initial focus will be on four states viz. Bihar, West Bengal, Jharkhand and UP.

Question 2. Look up for VL in HIV infected patients?

Answer The medical officers at ART centres in endemic states should be sensitized and trained to suspect for VL in all HIV positive individuals having fever >2 weeks duration, hepatosplenomegaly and pancytopenia from an endemic area. Such patients should be referred for VL testing with rk-39 (RDT). Those with rk-39 positivity should be immediately linked to facility where VL treatment is available. Those with rk-39 negative but high clinical suspicion for VL should undergo Bone marrow aspiration for confirmation of diagnosis as per algorithm **(Annexure II).**

Question 3. Diagnostic criteria for VL in HIV infected patients?

Answer The diagnosis of VL in HIV infected patients is done as for those who are HIV negative (rk-39 positive tests followed by Bone marrow/spleenic aspirate). Since rk-39 may not be positive in all HIV co-infected patients due to low immunity, those with rk-39 negative but high clinical suspicion for VL should also undergo Bone marrow aspiration and further required investigations for confirmation of diagnosis as co infected patients may be rk39 negative but harbouring the infection

Question 4. Can VL be taken as AIDS defining illness in the Indian context?

Answer Atypical disseminated leishmaniasis is an AIDS defining illness (WHO clinical stage IV). However VL as such is not defined as AIDS defining illness in Indian national HIV/AIDS programmes (In Africa, Sudan, Brazil and Kenya this is taken as AIDS defining illness). The group recommended that it should be discussed further with NACO/ WHO on inclusion of VL as an AIDS defining illness.

Question 5. ***Can we treat all HIV- VL co-infected persons with ART irrespective of CD_4 counts?***

Answer Though, VL is not an AIDS defining illness the group felt that considering the fact that 79 to 97% of VL patients will relapse , if not started on ART, it was recommended that all HIV- VL co-infected persons with ART irrespective of CD_4 counts. This will be discussed in NACO TRG on ART for approval

Question 6. ***Are WHO recommendations of single dose Ambisome 10mg/kg body weight enough for HIV-VL co-infected patients or do we need higher dosages or combination therapy?***

Answer The group had lot of discussion on dosing for Ambisome in HIV-VL co-infected patients, particularly in view of RMRIMS-MSF study at Hajipur (Vaishali, Bihar). However considering that there are no control studies, it was decided to adopt WHO guidelines on treatment of HIV-VL co-infected patients (40 mg/kg body weight as total dose, **3-5 mg/kg daily or intermittently for 10 doses, days 1-5, 10, 17, 24, 31 and 38).** It was decided to use Ambisome in all 54 districts including 4 districts where it is not proposed to be used for VL.

Question 7. ***Is there any need for secondary prophylaxis?***

Answer At the moment there is insufficient evidence to recommend secondary prophylaxis. Moreover, there were concerns about resistance in case secondary prophylaxis because of low dosages used.

Question 8. ***When to start ART - after VL treatment or simultaneously?***

Answer It was decided to start VL treatment immediately and ART to be started after 7-10 days once the patients has been adequately counselled and prepared for life-long ART.

Question 9. ***What would be the coordination mechanism between NACP and NVBDCP programme for HIV-VL co-infected patients?***

Answer It was recommended that strong coordination mechanism be established between NACP and NVBDCP at national level as well as at state level in these 4 states. For proper coordination M & E tools be developed for tracking the HIV-VL co-infected patients and regular reporting (on the lines of HIV-TB coordination mechanism). The state VBD officer should be involved in review meeting of ART centre at SACS level. It was also decided that HIV- VL co-infected patients should be immediately tracked by outreach workers of Care and Support centres (NACO) and brought back for adequate treatment.

Question 10. How to treat patients presenting with a relapse to 40mg/kg Ambisome?
Answer Since these patients are going to have multiple relapses even after HAART, best option is to retreat them with AmBisome (40 mg/kg). Presently there is no recommendation for combination therapy and further evidence is needed

As per suggestion by Dr Dhariwal, following operational Research studies were also agreed to be conducted.

1. Implementation Research for management of HIV-VL co-infection as per guidelines.
2. Transmission dynamics of the HIV in VL cases.

The meeting ended with vote of thanks to the chair.

Annexure - I

First Meeting of working group on HIV and Kala Azar in India

1st September 2014, RMRI, Patna, Bihar

10.00- 13:00 Hrs	**Session 1**	
	Opening address Dr A S Rathore, DDG CST NACO	10 min
	Welcome Address Dr AC Dhariwal, Director, VBDCP GoI	10 min
	VL in India Dr Pradeep Das, Director, RMRI	30 min
	HIV in India and Bihar—current status Dr. B B Rewari, NPO (ART) WHO	20 min
	MSF experience of VL-HIV infection in Bihar Dr Sakib Burza	30 min
	Diagnosis of VL in the setting of co-infection PK Sinha	30 min
	Treatment of VL in co-infection Krishna Pandey	30 min
	ARV in the National Programme Shyam Sundar	30 min
13.00-14.00	**Lunch Break**	
14:00-16:00 Hrs	**Session 2**	
	WHO guidelines on HIV -VL Co infection Dr Saurabh Jain	30 min
	Discussion on Diagnosis of HIV in VL patients and further management strategies All participants	30 min
	Summary of discussion and way forward Dr BB Rewari, NPO(ART)	20 min
	Closing remarks Dr A C Dhariwal, Director, VBDCP	

Annexure - II

Annexure II: Diagnostic and treatment algorithm for HIV patients with suspicion of VL